

Appendix B

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:Laguens *et al.*

Art Unit: 1633

Application No: 10/714,449

Examiner: Kaushal, Sumesh

Confirmation No: 9366

Filed: November 17, 2003

Atty. Docket No:

For: METHOD TO INDUCE NEOVASCULAR
FORMATION AND TISSUE
REGENERATION

Customer No:

26694
PATENT TRADEMARK OFFICE**DECLARATION UNDER 37 C.F.R. 1.132**

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, Roger Laham, declare as follows:

1. I am an expert in the field of cardiology and heart angiogenesis.
2. My credentials are set forth in my CV, which is attached. I have no relationship with Bio Sidus S.A., the owner of Sterrenbeld Biotechnologie North America Inc., or with Fundacion Universitaria Dr. Rene G. Favaloro, which I understand is co-owner of the patent application.
3. I have read the claims under consideration and am familiar with the application identified above. In particular, I am aware that broad claim 1 (as modified in a Reply to the Office Action dated February 5, 2008) is:

Claim 1 (currently amended). A method for inducing cardiomyogenesis, comprising administering to a cardiomyocyte or tissue comprising cardiomyocytes in need thereof a dose of a polynucleotide that encodes the vascular endothelial growth factor, VEGF 1-165,

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wherein the coding sequence is operably linked to a CMV promoter and is in a plasmid vector, the dose being sufficient to induce cardiomyogenesis.

4. I have reviewed the Office Action dated October 5, 2007, particularly pages 6-9 directed to "Claim Rejections - 35 USC 102/103," and I have read the Vale *et al.* (2000) *Circ.* 102, 965-974 (Vale *et al.*) reference cited by the Examiner in the Office Action.
5. It is my understanding that the Examiner is of the opinion that the claims are rendered obvious by the Vale *et al.* reference. The Examiner apparently believes that the Vale *et al.* reference teaches a gene therapy method that assesses the efficacy of phVEGF(165) gene transfer in chronic myocardial ischemia.
6. However, it is my understanding, upon reading Vale *et al.*, that the reference merely shows that the administration of low levels of a plasmid encoding VEGF 1-165 can augment perfusion of ischemic myocardium and can restore some function to the ischemic tissue, not that the administration of the low levels of plasmid can induce cardiomyogenesis. The reference shows that administration of 500 µg of a plasmid encoding VEGF 1-165 improved perfusion of the aforementioned ischemic myocardial tissue, which was accompanied by improvement of regional myocardial function (*i.e.* NOGA linear shortening of the ischemic area). As I read it, the reference does not suggest or disclose that the dose of VEGF 1-165 which is administered therein is effective to induce cardiomyogenesis (mitosis or proliferation of the cells, which can, *e.g.*, lead to the replacement of dead cells in an infarcted area), or that it was uncovered or detected. The higher dose probably resulted in the invention described and included in the claims.
7. It is also my understanding that the Examiner is of the opinion that the present inventors merely discovered an optimum or workable range of dosages of the VEGF plasmid by routine experimentation; and that the modification was within the capabilities of one skilled in the art.
8. However, based on my extensive experience in the field, it is my opinion that the results reported in Vale *et al.* - that a relatively low dose of VEGF plasmid can increase myocardial function (of cells that are ischemic, but not infarcted) - is qualitatively different from the findings by the present inventors that a relatively high dose of VEGF plasmid is actually able to induce cardiomyogenesis, which leads to an increase in the number of cardiomyocytes in the treated tissue and a consequent

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replacement of cells, e.g. in an infarcted (dead) area of the treated tissue. The induction of cardiomyogenesis is a completely different phenomenon from merely increasing myocardial function via reperfusion of the affected tissue. As I read it, the method of Vale *et al.* would not necessarily have led to the stimulation of cardiomyogenesis.

9. Moreover, as one who has worked in the field of cardiology for many years, it is my opinion that at the time of the effective filing date of the application (May 15, 2001), it could not have been predicted whether one would be able to induce cardiomyogenesis by *any* method of gene therapy, let alone by introducing nucleic acid encoding VEGF, a protein which, until the time of the present invention, was only thought to act as a growth factor for endothelial cells (not for cardiomyocytes). I would not have expected one to be able to obtain the striking results shown by the inventors in the patent application.

10. It is also my belief that other experts in the field of cardiology would have found the results shown by the inventors in the patent application to be unexpected, and would have understood that the method of Vale *et al.* would not necessarily have lead to the stimulation of cardiomyogenesis.

11. The ability to induce cardiomyogenesis provides advantages over methods that merely rescue ischemic or hibernating (but not dead) myocardial tissue, e.g. by enhancing reperfusion of the tissue. For example, the stimulation of cardiomyogenesis allows for the treatment of heart failure, myocardial infarction, and other conditions.

12. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the above-referenced application or any patent issuing thereon.

Date:

2/28/08

DOCS #914605/v5


Roger Laham, MD

PART I: General Information

DATE PREPARED: December, 2006

Name: Roger Laham

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East Campus, SL 423C
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Brookline, MA 02445

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Education:

1982 Baccalaureate College des Frères Sacré-Coeur

1985 B.S. American University of Beirut

1989 M.D. American University of Beirut

Postdoctoral Training:

Internships and Residencies

1989-1990 Intern, Department of Medicine
Duke University Medical Center, Durham, NC

1990-1991 Junior Resident, Department of Medicine
Duke University Medical Center, Durham, NC

1991-1992 Senior Resident, Department of Medicine
Duke University Medical Center, Durham, NC

Clinical and Research Fellowships

1992-1994 Clinical Fellow, Cardiovascular Division
BIH, Harvard Medical School, Boston, MA

1994-1996 Clinical Fellow, Interventional Cardiology Section
BIH, Harvard Medical School, Boston, MA

1994-1996 Fellow, Angiogenesis Research Center
 BIH, Harvard Medical School, Boston, MA

Licensure and Certification:

1989, 1992, 1994 Certified, Advanced Cardiac Life Support
1996, 2001, 2004 American Heart Association

1992 Diplomat, American Board of Internal Medicine
 Internal Medicine

1992-present State of Massachusetts Medical License

1995 Diplomat, American Board of Internal Medicine
 Cardiovascular specialty

1999 Diplomat, American Board of Internal Medicine
 Interventional Cardiology

2004 Recertified, American Board of Internal Medicine
 Internal Medicine

2005 Recertified, American Board of Internal Medicine
 Cardiovascular specialty

Academic Appointments:

1992-1995 Clinical Fellow in Medicine
 Harvard Medical School, Boston, MA

1995-1999 Instructor in Medicine
 Harvard Medical School, Boston, MA

1999-2002 Assistant Professor of Medicine
 Harvard Medical School, Boston, MA

2002- Associate Professor of Medicine
 Harvard Medical School, Boston, MA

2005- Faculty, Harvard Stem Cell Institute

2005- Faculty, CEC Committee,
 Harvard Clinical Research Institute, Boston, MA

Hospital Appointments:

1999	Assistant Director, Interventional Cardiology BIDMC, Boston, MA
1999-2001	Director, Clinical Research Angiogenesis Research Center BIDMC, Boston, MA
2000-present	Director, Basic Angioplasty Research Interventional Cardiology Section BIDMC, Boston, MA

Major Committee Assignments:

1988-1989	Member, Continuing Education Committee American University
1995-1996	Member, Committee on Bylaws Massachusetts Medical Society
1998-2005	Member, Committee on Clinical Investigation BIDMC, Boston, MA
2000-2005	Delegate, Massachusetts Medical Society
2000-2002	Scientific Committee and Course Co-director, Vienna Annual Interdisciplinary scientific congress
2001-present	Scientific Committee, International Congress on Coronary Artery Disease
2000-present	Scientific Committee, International Coronary artery Disease Congress
2001-present	International Referee, Biomedical Research Council, Singapor
2002-present	National Referee, Department of Defense Research Program, Breast Cancer study section
2002-present	Society of Cardiac Angiography and Interventions Credentials Committee
2003-present	Reviewer for the NHLBI Program of Excellence in Gene Therapy (PEGT) National Cores

2003	Reviewer, GlaxoSmithKline fellowship Research and Development Fellowship Program
2004	Reviewer FDA intramural program
2005	Reviewer for the NHLBI study section on cell based therapy

Professional Societies:

1993	Member, Massachusetts Medical Society
1993	Member, American Medical Association
1994	Member, American College of Physician
1994	Member, American College of Cardiology
1998	Member, American Association for the Advancement of Science
1998	Member, American Heart Association Council on Atherosclerosis, Thrombosis, and Vascular Biology
1999	Member, Society for Cardiac Magnetic Resonance Imaging
2000	Delegate, Massachusetts Medical Society
2001	Fellow, American Heart Association Council on Atherosclerosis, Thrombosis, and Vascular Biology
2002	Fellow of American Society for Cardiovascular Angiography and Interventions (FSCAI)
2002	Member, American Association for Advancement of Science
2003	Fellow of the American College of Cardiology (FACC)
2005	Member, Society for Vascular Medicine and Biology
2006	Faculty, Harvard Stem Cell Institute
2006	Fellow, American Heart Association Council on Cardiovascular Radiology and Intervention

Editorial Boards:

1998-present	Associate Editor Interventional Cardiology	Uptodate in Medicine Wellesley, MA
1999-present	Editorial Board	Cardiac and Vascular Regeneration
1998-present	Editorial Board	CHF Disease Management
1998-present	Editorial Board	Complementary Therapies in Chronic Care
2002-present	Editorial Board	Catheterization and Cardiovascular Interventions

2003-present	Editorial Board	Cardiovascular Radiation Medicine
1999-present	<i>Ad-hoc reviewer</i>	<i>Circulation</i>
1999-present	<i>Ad-hoc reviewer</i>	<i>Journal of the American College of Cariology</i>
1999-present	<i>Ad-hoc reviewer</i>	<i>Catheterization and Cardiovascular Intervention</i>
2000-present	<i>Ad-hoc reviewer</i>	<i>Clinical and Experimental Immunology</i>
2000-present	<i>Ad-hoc reviewer</i>	<i>American Journal of Cardiology</i>
2000-present	<i>Ad-hoc reviewer</i>	<i>Cardiac and vascular regeneration</i>
2001-present	<i>Ad-hoc reviewer</i>	<i>Journal of Pharmacology and Experimental Therapy</i>
2001-present	<i>Ad-hoc reviewer</i>	<i>New England Journal of Medicine</i>
2001-present	<i>Ad-hoc reviewer</i>	<i>American Heart Journal</i>
2001-present	<i>Ad-hoc reviewer</i>	<i>American Journal of Physiology</i>
2002-present	<i>Ad-hoc reviewer</i>	<i>The Lancet</i>
2002-present	<i>Ad-hoc reviewer</i>	<i>Am. J. of Cardiovascular Drugs</i>
2002-present	<i>Ad-hoc reviewer</i>	<i>Trends in Molecular Medicine</i>
2002-present	<i>Ad-hoc reviewer</i>	<i>Coronary Artery Disease</i>
2003-present	<i>Ad-hoc reviewer</i>	<i>Current gene therapy</i>
2003-present	<i>Ad-hoc reviewer</i>	<i>Gene Therapy (Nature)</i>
2003-present	<i>Ad-hoc reviewer</i>	<i>Diabetes</i>

2004-present	<i>Ad-hoc reviewer</i>	<i>Gene Therapy and Molecular Biology</i>
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2004-present	<i>Ad-hoc reviewer</i>	<i>Circulation Research</i>
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Awards and Honors:

1982-1989	Dean's Honor List, American University of Beirut
1985	Bachelor of Sciences with High Distinction, American University of Beirut
1987-88	Franklin Thomas Moore-Ethel Jessup Memorial Prize American University of Beirut
1987-88	Munib Shahid Prize, American University of Beirut
1989	Doctor of Medicine with Distinction, American University of Beirut
1989	Penrose Award (for the best combination of the qualities of scholarship, character, leadership, and contribution to the University as a whole), American University of Beirut
1993-1996	Physician's Recognition Award, American Medical Association
1994-1995	Hewlett-Packard Fellowship Award in Cardiovascular Research
1995	American College of Cardiology/Bristol-Myers Squibb Affiliate Travel Award
1996-1999	Physician's Recognition Award, American Medical Association
1996	The Altman Award Endowment Fund for Outstanding Talent as Clinician, Researcher, and Humanitarian Deliverer of Care, BIH, Boston, MA
1996	Pharmaceuticals Travel Award
1999	Plenary Lecture, Transcatheter Therapeutics Symposium
2001	Plenary Lecture, Vienna Interdisciplinary Symposium
2001	Plenary Lecture, Moscow Cardiology Summit
2001	Plenary Lecture, American Heart Association meeting, Rockport, Maine
2001	Plenary Lecture, Cardiac Magnetic Resonance Imaging Society Scientific Session
2001	Keynote speaker, International Congress on Coronary artery disease
2002	GCRC Award, presented at GCRC/NCRR annual meeting in Baltimore, MD
2002	Allen Ephraim Diamond Lecturer (Keynote address), Toronto
2003	Stafford Cohen development award
2005	Dean's International Council, University of Chicago Harris School of Policy

Patents:

- 2004- METHODS AND COMPOSITIONS FOR TREATING
CONDITIONS INVOLVING ABNORMAL ANGIOGENESIS
USING RTEF-1-FILED
- 2005- METHODS TO EXCLUDE LEFT ATRIAL APPENDAGE IN
TREATMENT OF ATRIAL FIBRILLATION-FILED
- 2006- DEVICES AND METHODS FOR TISSUE TRANSPLANT AND
REGENERATION-FILED
- 2006- DEVICES AND METHODS FOR CARDIAC
RESTRAINT AND TREATMENT OF HEART DILATION AND
FAILURE-FILED
- 2006- DEVICES AND METHODS FOR PERCUTANEOUS VALVE
REPLACEMENT-FILED

Part II: Research, Teaching, and Clinical Contributions:

A. Narrative:

Teaching: Teaching responsibility has involved mainly the supervision and instruction of nurse practitioners, medical students, housestaff, and fellows in the division of cardiology at BIDMC, and at Harvard Medical School in clinical cardiology, interventional cardiology, and clinical angiogenesis research. Teaching has involved 7 nurse practitioners, 20 medical interns and residents, and 8 medical students that are rotating through the clinical services attended, including the coronary care unit and the cardiology units. This also included lectures given to medical interns, residents, cardiology fellows and medical students about interventional cardiology and angiogenesis. The number of hours spent yearly preparing and delivering these teaching responsibilities approximates 7 hours weekly, including the yearly cardiovascular exam teaching to second year medical students.

Other teaching contributions include the instruction of physician in the U.S., Canada, Europe and the Middle East in performing advanced interventional procedures including electromechanical left ventricular mapping, various Atherectomy techniques, crossing total occlusions, intramyocardial injections, distal protection, high risk interventions. I serve as a mentor to a number of trainees. I also serve on the scientific committee of several teaching courses for medical professionals nationally and internationally.

Research: Since joining the fellowship program and then the faculty rank BIDMC/Harvard Medical School, my research activities centered on translational research in vascular biology, angiogenesis, myogenesis, and new device development. These efforts have taken the form of basic research projects focused on restenosis and the endothelial responses to angiogenic growth factors, animal research projects focused on physiologic assessment of coronary angiogenesis in porcine models of myocardial ischemia and murine models of acute myocardial infarction, drug delivery research, cell based therapy, microtissue transplantation, and finally clinical trials testing efficacy of angiogenic growth factors in patients with advanced coronary disease. My research was funded by a Hewlett-Packard fellowship award (1995), a career development award program (CAP) from the General Clinical Research Center, NCCR (1997-2000 and then 2000-2002), a project I lead in a SCOR program (2000-2005), as well as industry funding. Eight of my former trainees now hold faculty rank in academic institutions in the US and abroad and every one of my trainees have had research presentations at major national meetings (AHA, ACC, TCT, etc.). My current basic research efforts are concentrated on understanding the mechanism of action of novel angiogenic cytokines in vitro (matrigel models and migration assays) and in vivo using small animal models of myocardial infarction (mouse MI model), microorgan, myotissue transplantations and cord blood transplantation. The use of the mouse MI model allows a better understanding of the steps needed for functionally significant angiogenesis by using mice lacking key genes in the angiogenic cascade (enos knockout,...) with selective expression of certain genes in the heart (transgenic models). I am assisted in this work by one postdoctoral fellows and Dr. Jian Li (Assistant Professor), who acts as an advisor on

these studies. We are currently investigating the role of exercise in the development of collaterals and overexpression of FGF and VEGF and their receptors in mice models of myocardial infarction. In addition, SDF-1, Cord blood derived stem cell, APC, microorgans, myotissue, cardiac stem cells are ongoing. Large animal studies have recently focused on local delivery of angiogenic agents to the heart, but more recently, we are investigating cell based therapy and microtissue transplantation in large animal models for myocardial regeneration and myocardial ischemia. This work will be the basis of an investigator/industry sponsored IND/IDE for the investigation of cell based therapy for heart failure. I am assisted in this project by a post-doctoral fellow and a surgical resident. An upcoming project which will involve basic, preclinical, and clinical experimentation is investigating the effect of B-Natriuretic peptide on endothelial function and proliferation, coronary microvascular resistance, coronary blood flow, and epicardial tone. I am the principal investigator on several clinical studies including new device trials and angiogenesis trials. My research efforts have been recognized by my peers as publications in several peer-reviewed journal as well as presentations at most National and International meetings in Cardiology. I have delivered several keynote and plenary presentations and was invited to deliver the opening lecture at the International CAD meeting and I am asked to review manuscripts and grant proposals from several prestigious journals and funding agencies.

B. Research Funding:

Past:

1994-1995	Hewlett-Packard Fellowship Award Program Biology of atherosclerosis	Principal Investigator
1997-2000	NIH-GCRC CAP Award, MO1-RR01032 Therapeutic angiogenesis using FGF-2	Principal Investigator
1996-1998	Genentech Inc. Preclinical evaluation of VEGF	Co-Investigator
1997-1998	Chiron Inc. Preclinical evaluation of FGF-22	Co-Investigator
1997-1998	Genentech Inc. Intracoronary and intravenous VEGF in Patients	Co-Investigator
1999-2004	Biosense Inc., Johnson and Johnson Magnetic resonance imaging in angiogenesis	Principal Investigator
1998-1999	Chiron Inc. Phase I study of FGF-2	Co-Investigator
2000-2002	NIH-GCRC CAP Award extension, RR01032 Study of outcome measures in angiogenesis	Principal Investigator
1999-2002	Biosense Inc., Johnson and Johnson Direct Myocardial Revascularization	Principal Investigator
1998-2002	Chiron Inc. Phase II intracoronary bFGF	Principal Investigator

2001-2003	Diacrin Inc. Cell transplantation for angiogenesis	Principal Investigator
2001-2002	Cook Interventional LOGIC study of COOK stent	Principal Investigator
2001-2002	Jomed Inc. Barricade study of Jomed stent	Principal Investigator
2001-2002	Berlex Laboratories Inc. Intracoronary adenoviral-FGF-4 for angiogenesis	Principal Investigator
2001-2002	Transvascular Inc. Transvenous myocardial delivery	Principal Investigator
2002-2004	Valentis Inc. Plasmid-Del-1 delivery for ischemic heart disease	Principal Investigator
2002-2004	Vascular Genetics Inc. Plasmid VEGF-2 Myocardial Angiogenesis study	Principal Investigator
2002-2004	Scios Inc. Microvascular and signaling pathways of Natrecor	Principal Investigator
2002-2003	Scios Inc. Effects of Natrecor on Coronary Circulation	Principal Investigator
2000-2005	Project V of NIH Ischemia SCOR, HL 63609 Therapeutic angiogenesis in patients	Principal Investigator
2000-2002	Cardiovascular Therapeutics CARISA study in patients (Ranolazine)	Principal Investigator

Current:

2002-2007	NIH/NHLBI-1RO1HL69024-01A1 (Sellke PI). Surgical Intramyocardial Angiogenesis in a Swine Model of hypercholesterolemia	Co-Investigator
2003-2006	Skin Microorgan role in inducing angiogenesis, BIRD Foundation	Principal Investigator
2004-2006	Preclinical assessment of the Triactive Device, Kensey nash	Principal Investigator
2005-2007	Clinical Trial of ranolazine in unstable angina, TIMI-36, Merlin study	Principal Investigator
2006-2008	Clinical trial of spinal cord stimulation for refractory angina, ANS, Dallas, TX	National Principal Investigator
2006-2008	Clinical trial of Plasmid-VEGF 165 using intramyocardial injections in patients with end stage coronary disease, Corautus Genetics, Atlanta	Principal Investigator
2005-2008	Core 64, multislice CT angiography compared to angiography for detection of CAD, Toshiba, Japan	Co-Principal Investigator
2007-2008	CIMIT Proof Of Principle Award on Myotissue tranplantation, Boston, MA	Principal Investigator
2007-2008	MTTC new aortic valve design, Boston, MA	Principal Investigator

C. Research Activity:

Bench Research:

1996-1998	Intracoronary, local delivery, and perivascular angiogenic effect of VEGF	Co-Principal Investigator: Designed and conducted experiments in animal models
1997-1999	Role of bFGF in limiting infarct size after experimental coronary ligation in mice: mechanisms and potential therapeutic benefit	Co-Principal Investigator: Designed and conducted experiments in animal models
1998-1999	Intrapericardial bFGF in a large animal model of myocardial ischemia	Co-Principal Investigator: Designed and conducted experiments in animal models
1999-2001	Tissue and myocardial distribution and retention of heparin-binding growth factors after intracoronary, intravenous, and intrapericardial delivery	Principal Investigator: Conceived, proposed, designed, and conducted experiments in animal models
1999-2001	Tissue and myocardial distribution and retention of heparin-binding growth factors after intramyocardial delivery	Principal Investigator: Conceived, proposed, designed, and conducted experiments in animal models
2000-2001	Tissue and Myocardial distribution of growth factors and gene therapy vectors after angiosense delivery	Principal Investigator: Conceived, proposed, designed, and conducted experiments in animal models
2001	Epicardial versus adenoviral delivery of VEGF ₁₂₁	Principal Investigator: Conceived, proposed, designed, and supervised experiments in animal models
2000-2001	Angiogenic efficacy of aFGF in a porcine ameroid constrictor model	Co-Principal Investigator: Conceived, proposed, designed, and supervised delivery experiments in animal models
2001	Evaluation of a novel Angiojet thrombectomy device	Principal Investigator: Conceived, proposed, designed, and supervised experiments in animal models
2001-2002	Evaluation of autologous myoblast transplant for ischemic heart disease and congestive heart failure	Principal Investigator: Conceived, proposed, designed, and supervised experiments in animal models
2001-2002	Study of effect of exercise on myocardial angiogenesis and myocardial expression of angiogenic cytokines in a mouse model of myocardial infarction	Principal Investigator: Conceived, proposed, designed, and supervised experiments in animal models
2002-	Study of effect of BNP (Natreacor) on endothelial cell proliferation and migration	Principal Investigator: Conceived, proposed, designed, and supervised experiments
2002-	Effects of Stromal Derived Factor-1 on stem cell trafficking in mouse model	Principal Investigator: Conceived, proposed, designed, and supervised experiments
2002-	Study of microvascular effects and signaling pathways of BNP (Natreacor) using isolated microvessels	Principal Investigator: Conceived, proposed, designed, and supervised experiments
2003-	Study of Triactive system novel design,	Principal Investigator: Conceived,

	Kensley Nash	proposed, designed, and supervised experiments
2003-	Characterization of cord blood for angiogenesis/myogenesis as stem cells	Principal Investigator: Conceived, proposed, designed, and supervised experiments
2003-	Microtissue transplantation (skin microorgans) for angiogenesis, BIRD foundation	Principal Investigator: Conceived, proposed, designed, and supervised experiments
2004-	Microtissue transplantation (autologous myocardial tissue) for myogenesis	Principal Investigator: Conceived, proposed, designed, and supervised experiments
2004-	Investigation of AV graft model of restenosis and failure	Co-Investigator: assisted in development of protocol and IVUS imaging
2004-	Hypercholesterolemia model of myocardial ischemia	Co-Investigator: assisted in development and conduct of protocol
2005-	Decellularization protocol in myotissue transplantation	Principal Investigator: Designed and supervised protocol
2006-	Myogenesis using cardiac stem cells	Principal Investigator: Designed and supervised protocol

Outcome Research:

1999-	Use of magnetic resonance imaging in clinical angiogenesis studies	Co-Principal Investigator: Conceived, proposed, designed, and supervised experiments in animal models
1998-2001	Use of magnetic resonance imaging in clinical laser myocardial revascularization studies	Principal Investigator: Conceived, proposed, designed, and supervised experiments
1999-2002	Use of BIOSENSE NOGA mapping as an outcome measure in angiogenesis studies	Principal Investigator: Conceived, proposed, designed, and supervised experiments
2001-	Outcome in no-option patients	Principal Investigator: Conceived, proposed, designed, and supervised experiments
2002-	Placebo effect in Cardiovascular disease	Principal Investigator: Conceived, proposed, designed, and supervised experiments

Clinical trials: (Most of the current clinical trials are also listed in current funding)

1994-1996	Metoprolol in Dilated Cardiomyopathy Trial: Multicenter trial of metoprolol in heart failure	Co-Investigator: Analyzed and collected data on enrolled patients
1995-1997	Flopan therapy in congestive heart failure: Multicenter trial of a novel inotrope in heart failure	Co-Investigator: recruited and enrolled patients and collected data

1995-1997	Respit Trial (OPC 18790 use in congestive heart failure): Multicenter trial of a novel inotrope in heart failure	Co-Investigator: recruited and enrolled patients and collected data
1996-2001	bFGF angiogenesis trial. Single center investigator initiated trial of basic fibroblast growth factor for therapeutic angiogenesis	Co-Principal Investigator: Helped conceive, propose, design, and conduct clinical trial experiments
1997-1998	Intracoronary rhVEGF angiogenesis trial: Multicenter phase I study of vascular endothelial growth factor in patients with ischemic heart disease,	Co-Investigator: submitted regulatory documents, recruited and enrolled patients and collected data
1997-1999	Hu23F2G for AMI with primary angioplasty: Multicenter trial of a novel inflammation inhibitor in acute myocardial infarction	Co-Investigator: submitted regulatory documents, recruited and enrolled patients and collected data
1998-1999	Intravenous rhVEGF angiogenesis trial: Multicenter phase I study of vascular endothelial growth factor in patients with ischemic heart disease	Co-Investigator: submitted regulatory documents, recruited and enrolled patients and collected data
1998-1999	rFGF-2 angiogenesis study: intracoronary/intravenous/PhaseII: Multicenter phase I-II study of basic fibroblast growth factor in patients with ischemic heart disease,	Co-Investigator: helped design study with sponsor, carried out preclinical evaluation, submitted regulatory documents, recruited and enrolled patients and collected data
1998-2000	Betacath denovo and in-stent restenosis radiation study: Multicenter study of beta radiation in the prevention of restenosis	Co-Investigator: recruited, enrolled, and followed patients
1998-2000	VEGAS II study: Multicenter study of a novel thrombectomy device to remove clot from coronary and venous conduits	Co-Investigator: recruited, enrolled, and followed patients
1998-2000	SAFER study: Multicenter study of a distal occlusion device to guard against embolization and no-reflow after angioplasty	Co-Investigator: recruited, enrolled, and followed patients
1998-1999	SPORT study: Multicenter study of rotational atherectomy in coronary arteries	Co-Investigator: recruited, enrolled, and followed patients
1998-1999	AMIGO study: Multicenter study of directional coronary atherectomy in heart disease	Co-Investigator: recruited, enrolled, and followed patients
1998-2001	DIRECT study: Multicenter study of BIOSENSE-guided laser myocardial revascularization in patients with severe coronary artery disease	Co-Principal Investigator: Helped conceive, propose, design, and conduct clinical trial
1998-2001	Halt-MI study: Multicenter study of a novel inhibitor to reduce reperfusion injury after myocardial infarction	Co-Investigator: recruited, enrolled, and followed patients
1999-2001	Park-Davis Intramyocardial injection trial:	Principal Investigator: Helped conceive,

	Multicenter study of the intramyocardial injection of an adenoviral construct containing VEGF ₁₂₁ in patients with severe coronary artery disease	propose, design, and conduct clinical trial in three centers in the US
1999-2001	Cutting balloon registry in patients with coronary artery disease	Principal Investigator: Center PI with responsibility for patient enrollment and follow-up
2001-2002	Target study: Comparison of Reopro and Aggrastat for PCI,	Co-Investigator: recruited, enrolled, and followed patients
2001-	Subxyphoid Access of the Pericardium using a blunt tip needle,	Principal Investigator: conceived, proposed, designed, and supervised conduct of single center clinical trial
2001-	Ethanol Ablation in Hypertrophic Obstructive Cardiomyopathy	Co-Principal Investigator: conceived, proposed, designed, and supervised conduct of single center clinical trial
2001-2002	ESPRIT trial: Comparison of Integrilin vs placebo in PCI	Co-Investigator: recruited, enrolled, and followed patients
2001-	CARISA study to evaluate Ranolazine in patients with angina	Principal Investigator: site PI, supervised conduct of multicenter clinical trial at BIDMC
2001-	Cardioseal closure device in patients with patent foramen ovale and cryptogenic stroke	Principal Investigator: conceived, proposed, designed, and supervised conduct of single center clinical trial of an HDE device
2001-	Cardioseal closure device in patients with ventricular septal defect	Principal Investigator: conceived, proposed, designed, and supervised conduct of single center clinical trial of an HDE device
2001-	Magnetic Resonance Imaging in Coronary Artery Disease	Principal Investigator: conceived, proposed, designed, and supervised conduct of single center clinical trial. Obtained funding
2001	Magnetic Resonance Imaging in Angiogenesis and Laser Myocardial Revascularization study	Principal Investigator: conceived, proposed, designed, and supervised conduct of single center clinical trial. Obtained funding
2001-	Use of Relaxin in patients with ischemic cardiomyopathy	Principal Investigator: conceived, proposed, designed, and supervised conduct of single center clinical trial, trial still not started
2001-	Magnetic Resonance Imaging in patients undergoing therapeutic Angiogenesis with adenoviral VP-16-Hypoxia Induced factor-1	Principal Investigator: helped conceive, propose, design, and supervise conduct of study. Obtained funding
2001-	Evaluation of the Cook Incorporated Logic Coronary Stent	Principal Investigator: site PI, supervised recruiting and enrolling patients
2001-	Autologous myocyte cell transplantation in	Principal Investigator: helped conceive,

	patients undergoing CABG	propose, design, and supervise conduct of study. Carried out preclinical studies for clinical trial
2001-	Use of Jomed covered stent for vein graft interventions	Principal Investigator: site PI, supervised recruiting and enrolling patients
2002-	Use of Paclitaxel Coated stent to prevent restenosis, Patency Study	Principal Investigator: site PI, supervised recruiting and enrolling patients
2002-	Valentis Study, Plasmid based Del-1 delivery for ischemic heart disease	Principal Investigator: helped conceive, propose, design, and supervise conduct of three center study. Obtained funding
2002-	VEGF-2 Myocardial Angiogenesis study (VGI)	Principal Investigator: site PI, supervised recruiting and enrolling patients
2002-	FGF-4 adenoviral study for Angiogenesis	Principal Investigator: site PI, supervised recruiting and enrolling patients
2002-	Effects of Natreacor on Coronary Circulation (Scios):	Principal Investigator: helped conceive, propose, design, and supervise conduct of single center study. Obtained funding
2002-	Clinical study to elucidate mechanism of placebo effect	Principal Investigator: helped conceive, propose, design, and supervise conduct of single center study. Obtained funding
2003-	Cooling for myocardial infarction, INNER COOL study	Principal Investigator: site PI, supervised recruiting and enrolling patients
2003-	SISR study of brachytherapy vs drug eluting stents	Co-Investigator: recruited, enrolled, and followed patients
2003-	Protect, anticoagulation strategy for PCI	Co-Investigator: recruited, enrolled, and followed patients
2004	Cool MI, cooling for myocardial infarction	Co-Investigator: recruited, enrolled, and followed patients
2004	MERLIN study of ranolazine in unstable angina	Principal Investigator: site PI, supervised recruiting and enrolling patients
2004	SHOCK II study in shock patients	Co-Principal Investigator
2005	Core 64, multislice CT angiography compared to angiography for detection of CAD	Co-Principal Investigator: Site cardiology PI, supervised recruiting and enrolling patients
2006	Clinical trial of Plasmid-VEGF 165 using intramyocardial injections in patients with end stage coronary disease	Principal Investigator: site PI, supervised recruiting and enrolling patients
2006	Clinical trial of spinal cord stimulation for refractory angina	National Principal Investigator: helped conceive, propose, design, and supervise conduct of multicenter study.

D. Report of Teaching:

1. Local Contribution:

1992-2001	Medicine 502M.1A Clinical fellow (92-96), faculty (96-present) educator 4-6 third and fourth year medical students per year 40 preparation/contact hours/year
1992-2001	Medicine 502M.1B Clinical fellow (92-96), faculty (96-present) educator 4-6 third and fourth year medical students per year 40 preparation/contact hours/year
1998-2000	IN709M.Jb. Patient-Doctor II Faculty educator 12 second-year medical student per year 20 preparation/contact hours/year
1998-2001	Biosense NOGA training at BIDMC Faculty educator/proctor 12 national and international physicians per year 40 preparation/contact hours/year
2000	IN750M.J-Patient Doctor III Faculty tutor 12 third year medical students 92 preparation/contact hours
2001	Cardiology fellow training Faculty educator 20 Cardiology fellows 72 preparation/contact hours
2001	Medical Resident and Intern teaching in CCU and Cardiology Faculty educator 15 Medical housestaff and students 38 preparation/contact hours
2002	Nurse educational symposium Faculty educator 68 nurses 12 preparation/contact hours
2002	Medical Housestaff lecture series in CCU Faculty educator 6 Medical Housestaff and students 24 preparation/contact hours
2003	Medical Housestaff lecture series in CCU Faculty educator 6 Medical Housestaff and students 24 preparation/contact hours
2003	Nurse practitioners and fellows Faculty educator

2004	6 nurses, 12 fellows 12 preparation/contact hours Nurse practitioners and fellows Faculty educator
2004	6 nurses, 12 fellows 12 preparation/contact hours Medical Housestaff lecture series in CCU Faculty educator
2005	6 Medical Housestaff and students 24 preparation/contact hours Medical Housestaff lecture series in CCU Faculty educator
2005	6 Medical Housestaff and students 24 preparation/contact hours Nurse practitioners and fellows Faculty educator
2006	6 nurses, 12 fellows 12 preparation/contact hours Medical Housestaff lecture series in CCU Faculty educator 6 Medical Housestaff and students 24 preparation/contact hours

Local (BIDMC/HMS):

1998	Invited lecture, Therapeutic angiogenesis, General Clinical Research Center, Boston, MA
1998	Cardiology Seminar: Therapeutic angiogenesis, outcome measures, Chiron site visit, BIDMC, Boston, MA
1999	Cardiology Seminar: Harvard teaching hospitals combined interventional live course, Interventional Cardiology Meeting, Boston, MA
1999	Invited Seminar on Angiogenesis; Therapeutic Angiogenesis, MR Research Meeting, BIDMC, Boston, MA
1999	Angiogenesis/DMR, Joint Program in Nuclear Medicine Seminar Series at Harvard Medical School, Boston, MA
2000	BIDMC Research Symposium, Angiogenesis/DMR, Boston, MA
2000	BIDMC/Harvard Medical School cardiology grand rounds: Angiogenesis, Boston, MA
2000	Harvard Interventional Cardiology Course, The no-option patient, Boston, MA
2001	BIDMC nursing educational day, <i>Ethanol ablation for hypertrophic</i>

- cardiomyopathy*, BIDMC, Boston, MA
- 2002 Invited Speaker and Moderator, First GCRC Translational Research Series: *Angiogenesis, from Bench to Bedside*, BIDMC, Boston, MA
- 2002 Speaker, Fellowship education series, *Options for no-option patients*, BIDMC, Boston, MA
- 2003 Speaker, Fellowship education series, *Options for no-option patients*, BIDMC, Boston, MA
- 2004 Lecturer, Coronary care Unit lecture series, 7 lectures on management of critical cardiology patients
- 2004 Speaker, Fellowship education series, Ethanol septal ablation, BIDMC, Boston, MA
- 2005 Lecturer, Coronary care Unit lecture series, 5 lectures on management of critical cardiology patients
- 2006 Lecturer, Coronary care Unit lecture series, 5 lectures on management of critical cardiology patients

2. Regional:

- 1998 Cardiology Seminar: Massachusetts General Hospital. Clinical Angiogenesis. Boston, MA
- 1999 Medical Grand Rounds: Alternative Revascularization, Good Samaritan Medical Center, Brockton, MA
- 1999 Medical Grand Rounds: Glover Day conference, The No Option patient, Glover, MA, May 1999
- 2001 Speaker, 51st Annual American Heart Association meeting, *Treatment for no-option patients*, Rockport, Maine
- 2001 Speaker, Cardiology Grand Rounds, DHMC, Dartmouth Medical School, *Innovative interventional therapies*, Lebanon, New Hampshire
- 2001 Speaker, Medicine Grand Rounds, DHMC, Dartmouth Medical School, *Treatment of "no-option" patients*, Lebanon, New Hampshire
- 2002 Speaker, Landmark Community education, Landmark Hospital, *The future of Cardiovascular Care*, Rhode Island
- 2002 Gene therapy and cell based therapy conference: *Gene Therapy for Angiogenesis*, Cambridge, MA
- 2002 Novel devices in Cardiology, Le Meridien Hotel, Boston, MA
- 2004 Speaker, David Spodick Symposium, Worcester, MA
- 2005 Speaker and Discussant, BioCare non-invasive imaging conference, Waltham, MA

2005 Speaker, percutaneous valves for valvular heart disease, Harvard Clinical Research Institute, Boston, MA

3. National and International contributions:

1995 Cardiology Seminar: New Device Interventions, Michigan State University, East Lansing, MI

1996 Cardiology Seminar: Interventional Cardiology, Texas Tech University, Amarillo, TX

1996 Cardiology Seminar: Vascular Biology: The Bridge Between Molecular Biology and Interventional Cardiology, Marshall's University, Morgantown, WV

1996 Cardiology teaching series: A Prospective evaluation of the outpatient initiation of antiarrhythmic therapy. American College of Cardiology, ACCEL recording

1997 Cardiology Seminar: Interventional Vascular Biology, University of Maryland Medical System, Baltimore, MD

1998 Cardiology Seminar, TCT XI, Biosense NOGA mapping and Biosense guided laser myocardial revascularization, National Interventional Cardiology meeting, Washington, DC

1998 Cardiology Seminar: Biosense guided DMR, Cardiology Seminar, Swedish Hospital, Seattle, WA

1999 Cardiology Training Course, NOGA mapping, Tips and Tricks, Ethicon J&J Training Site, Cincinnati, OH

1999 Course Director: Cincinnati training in NOGA mapping, Role of NOGA mapping in Clinical Practice, Cincinnati, OH, April

1999 Cardiology Seminar: NOGA summit, Cardiology meeting on intracardiac navigation technology Washington, DC

1999 Invited lecture, Basic concepts in Angiogenesis, International meeting, American Society of Artificial Internal Organs Annual meeting, San Diego, CA

1999 Cardiology Seminar: Magnetic Resonance Imaging as an outcome measure in laser myocardial revascularization, International Cardiology Meeting, Angiogenesis and DMR meeting, WHC, Washington DC

1999 Invited lecture: Angiogenesis Update, Laser DMR: current perspectives, National Cardiology meeting, Santa Fe, Santa Fe, NM

1999 invited lectures: Angiogenesis from bench to bedside, Cordis Webster educational seminar, Philadelphia, PA

1999 Invited lecture: Angiogenesis: State of the science, St Michael's Hospital,

University of Toronto, Toronto, Canada

- 1999 Invited lecture: 2nd Annual Cardiac Cath Lab Government Cardiologist Meeting, Cordis, Miami, FL
- 1999 The Multivaried role of MRI in Cardiology: Plennary session, Transcatheter Cardiosvacular Therapeutics XI, Washington, DC
- 1999 Biosense NOGA validation: Transcatheter Cardiosvacular Therapeutics XI, Washington, DC
- 1999 Angiogenesis, State of the art, Cardiology Grand Rounds, Erie Medical Center, Erie, PA
- 1999 Angiogenesis in Interventional Cardiology, 2nd Vienna Interdisciplinnary Symposium, Vienna, Austria
- 1999 Fundamental Aspects of Angiogenesis, European Society of Hematology meeting, Paris, France
- 1999 Drug delivery, Angiogenesis consensus meeting, Angiogenesis Foundation, Atlanta, GA
- 1999 Magnetic Resonance imaging in heart disease Atlanta Cardiology Research Institute, Atlanta, GA
- 1999 Frontiers of Angiogenesis, Beijing Medical University, Beijing, China
- 2000 Transcatheter Cardiovascular Interventions, Future of Gene Therapy in Heart Failure, Intravascular and Perivascular Approaches to Angiogenesis, New Delhi, India
- 2000 EuroCVS, Laser Myocardial Revascularization, Magnetic Resonance Imaging in Laser Myocardial Revascularization, Den Haag, The Netherland
- 2000 Angiogenesis Consensus Meeting, MRI as an outcome measure in clinical angiogenesis studies, Anaheim, CA
- 2000 FDA consensus meeting on Angiogenesis/DMR: Angiogenesis from Bench to Bedside, MRI as an outcome measure in angiogenesis, MD
- 2000 St Michael's Hospital, University of Toronto, Initiation of intramyocardial injection program, Toronto, ON
- 2000 Hahneman University, Grand Rounds, Angiogenesis, fact or fiction, Philadelphia, PA
- 2000 NOGA training course, NOGA mapping the Laham way, Cincinnati, OH
- 2000 Middle East Medical Assembly, Angiogenesis/DMR: the no option patient, Beirut, Lebanon
- 2000 Angiogenesis/DMR, A critical review of TMR, Angiogenesis using FGF, Washington, DC
- 2000 Treatment of Ischemic Heart Disease in the Third Millennium,

- Angiogenesis in heart disease, Thessaloniki, Greece
- 2000 Novel treatments in Heart Disease, Alternative revascularization, Quebec, Canada
- 2000 Panel on angiogenesis: the future of Angiogenesis and Myocardial revascularization, Intervention 2000 meeting, Atlanta, GA
- 2000 State of the Art Imaging: Latest advances in Gated Cardiac MRI, WEBCAST and CYBERSESSION
- 2000 Session Chair and Gene therapy strategies for angiogenesis, 3rd International Congress on Coronary Artery Disease, Lyons, France
- 2000 Cost effectiveness of brachytherapy, 3rd International Congress on Coronary Artery Disease Cordis Concurrent Session, Lyons, France
- 2000 American Heart Association Scientific Session, Session moderator, New Orleans, LA
- 2000 Session Chairman, Clinical Angiogenesis, Speaker: Clinical Angiogenesis Review, Basics of gene therapy, 3rd International Interventional cardiology and cardiac surgery meeting, Vienna, Austria
- 2001 Speaker, Treatment of no-option patients, Kensey-Nash Advisory Board meeting, Philadelphia, PA
- 2001 Speaker, Session Chairman, American Heart Association Scientific Conference on Therapeutic Angiogenesis and Laser Myocardial Revascularization, *Delivery strategies for Angiogenesis, Direct Trial for Laser Myocardial Revascularization*, Santa Fe, New Mexico
- 2001 Speaker, American College of Cardiology, 50th Annual Scientific Session, *Outcome measures in Angiogenesis*, Orlando, Florida
- 2001 Speaker and proctor, *Cell based therapy for Angiogenesis*, Euroinject Initiation, Copenhagen, Denmark
- 2001 Speaker and moderator, *Delivery strategies for therapeutic angiogenesis*, Angiogenesis and DMR symposium, Washington, DC
- 2001 Orlando Interventional Meeting, *Live case transmission and faculty discussion*, Orlando, FL
- 2001 Speaker and moderator, TCT 2001, *Optimizing Routes of Administration for Biologic Therapies in Specific Disease Syndromes, Enabling Technologies and Routes of Administration, Clinical Effectiveness of Perivascular bFGF Delivery, Angiogenesis—Current Status and Future Directions, Live case demonstration, The Physiologic Basis of the Placebo Effect In No-Option Patients, Emerging Applications of Genomics in Interventional Cardiology*, Washington, DC
- 2001 Opening Lecture, Fourth International conference on Coronary artery disease, *Angiogenesis: the future*. Symposium on Angiogenesis *Delivery modalities in Myocardial angiogenesis*. Session Moderator *Angiogenesis*.

Prague, Czech Republic

- 2001 Invited Speaker and Moderator, First Interdisciplinary Conference on the Non-invasive treatment of coronary artery disease. Moscow, Russian Federation
- 2001 Invited speaker, Fifth annual scientific meeting: *Angiogenesis Theory and Practice, Gene Therapy for Cardiovascular Diseases*, Hong Kong, China
- 2002 Plenary Session on Interventional Magnetic Resonance Imaging, Society of Cardiac MR Scientific Session: *MR-assisted Gene Therapy*, Orlando, FL
- 2002 CRT 2002, Interventional Symposium: *Delivery modalities in Cardiology*, Washington, DC
- 2002 Orthodiagnostic Expert meeting panel: *Point of Care in Interventional Cardiology*, Newark, NJ
- 2002 AFMR 2002, GCRC 2002 scientific sessions: *Placebo effect in end stage ischemic heart disease*, Baltimore, MD
- 2002 Speaker and moderator, TCT 2002, *Optimizing Routes of Administration for Biologic Therapies in Specific Disease Syndromes, Enabling Technologies and Routes of Administration, Clinical Effectiveness of Perivascular bFGF Delivery, Angiogenesis— Update, Live case demonstration and discussion, Point Counterpoint debate: TMR, PMR: effect of sugar Pill, Intervention on totally occluded vein grafts: a challenge that should no longer be resisted*, Washington, DC
- 2002 Speaker, Plenary Session, Meeting of Lebanese association of Cardiologist and Cardiac surgeons, *No option patient treatment, Conquering restenosis: Drug eluting stents and Brachytherapy*, Beirut, Lebanon
- 2002 Speaker, Medical grand rounds, *Gene Therapy for Angiogenesis*, Beirut, Lebanon
- 2002 Speaker, Plenary session, Vienna Interdisciplinary symposium on cardiology and cardiac surgery, *Treatment of Vein graft disease, Gene therapy for angiogenesis (replacement speaker, missed meeting)*, Vienna, Austria
- 2002 Speaker, Plenary session, Cardiological Society of India meeting, *Role of brachytherapy in the era of drug eluting stents, Gene therapy for angiogenesis*, Cochin, India
- 2003 Speaker and Moderator, CRT2003, *Angiogenesis by perivascular delivery*, Washington DC
- 2003 Kensey Nash Scientific Advisory Board, *A History of Delivery Strategies for the Heart*, St Thomas, US Virgin Islands
- 2003 Speaker and moderator, TCT2003, Washington DC

2003	Speaker and moderator, Buones Aires Interventional meeting, Argentina 2003
2003	Speaker and moderator, Mexico City interventional congress, Mexico
2003	Speaker and moderator, 2 nd annual Bioassist meeting, Paris France
2003	Speaker and moderator, 5 th annual International CAD meeting, Florence, Italy
2003	Speaker and moderator, 3 rd annual International meeting on atherosclerosis, Washington DC
2003	Speaker, Society of Cardiac angiography and intervention, Boston, MA
2003	Speaker, American College of Cardiology annual meeting, Chicago, IL
2004	Speaker, Millenium seminar, Dallas, Texas
2004	Speaker, CCU rounds, BIDMC, Boston
2004	Speaker, Angiogenesis and Myogenesis symposium, Washington DC
2004	Speaker, University of Oklahoma Cardiology Grand rounds, Oklahoma city, OK
2004	Speaker, Oklahoma Cardiovascular Association meeting, Oklahoma city, OK
2004	Speaker, Cardiology Grand Rounds, Aiforce Hospital, San Antonio, TX
2004	Speaker, Cardiology Grand Rounds University of Texas at San Antonio VA, San Antonio, TX
2004	Speaker, Cordis Headquarters, Miami, Florida
2004	Speaker, Cardiology Grand Rounds, Dayton Cardiolog center, Dayton, OH
2004	Speaker, Cardiology Grand Rounds, Mt Sinai Hospital, Dayton, OH
2004	Invited speaker, Imaging of stem cell therapy, American heart Association Scientific session, New Orleans, LA
2005	Speaker, Minneapolis Heart Institute Cardiology Grand Rounds, Minneapolis, Minnesota
2005	Speaker, Methodist Hospital Grand Rounds, Minneapolis, Minnesota
2005	Invited speaker, meet the experts, American College of cardiology, Orlando, Florida
2005	Keynote address, Connecticut regional meeting, Hartford, CT: treatment of no option patients
2005	Keynote address, 24 th meeting of society of Toxicologic Pathology, Washington DC
2005	ANS advisory board meeting, spinal cord stimulation, design of a clinical

trial

2005	Percutaneous treatment of valve disease, Dubai International heart meeting, Dubai, UAE
2005	International academy of Cardiology: Myogenesis, Vancouver, BC, Session chair and speaker
2005	ACLS course CMC, Beirut, Lebanon
2005	Myogenesis: beyond cell therapy, 6 th International CAD meeting, Istanbul, Turkey
2005	TCT 2005, Ethanol Ablation for hypertrophic cardiomyopathy, SFA revascularization, Myotissue transplantation, Washington DC
2005	American heart Association Scientific Sessions, Cord Blood between ES cells and adult stem cells, cellular transdifferentiation, future of Cardiac surgery, Dallas, Tx
2006	Live Russia transmission, Treatment of no option patients, Harvard Medical School
2006	CRT 2006, Cord blood transplantation for myocardial repair, myotissue transplantation for myocardial regeneration, Washington DC
2006	Harvard Medical International Dubai City Medical meeting, Cardiology in next 10 years, CAD an update, Dubai, UAE
2006	TCT 2006, Lecturer, Speaker, and Discussant, Washington
2006	Prince Sultan Heart Center, Lecture on IVUS and PFO closure, Riyadh, Saudi Arabia
2007	Prince Sultan Heart Center, imaging symposium, Riyadh, Saudi Arabia
2007	Interventional meeting in Tunisia, digivoting session, Tunisia, Tunisia
2007	Lebanese course on revascularization, Beirut, Lebanon
2007	CRT 2007, bone marrow cell therapy, Washington, DC

4. Advisory and Supervisory Responsibilities in Clinical or Laboratory Setting:

Clinical

- Two days a week attending in the Catheterization laboratory with diagnostic, interventional, and peripheral vascular disease cases. Supervision of 3-4 cardiology fellows. 20 hours/week
- One Full day clinic every four weeks for general cardiology and evaluation of patients with end stage cardiac disease and peripheral Vascular Disease. 8 hrs/4 weeks.

- One weekend per 2 months and one weeknight a week covering Cardiac catheterization laboratory for urgent and emergent cases. Supervision of 2 fellows. 5 hours/week
- Four weeks of coronary care unit coverage and 4 weeks of CMI cardiology coverage. Supervision of cardiology fellows, 4 residents and interns, and 1-2 medical students. 60 hrs/week.
- Weekly cardiac catheterization conference, clinical cardiology conference educating divisional faculty and fellows. 1 hour/week.
- Monthly National/International meeting presenting clinical data and proctoring other physician on the use of new devices. 8 hours/month

Laboratory

- 400 square feet at BIDMC dedicated for vascular biology, cell culture, and molecular research. Supervise 1 post-doctoral fellows, 6 hours/week
- IACUC approved animal facility with 6 active animal protocols (small and large animals). Supervision of two postdoctoral fellows and one technician. 6 hours/week.
- Weekly laboratory meeting. 1 hr/week
- Monthly National/International meetings presenting novel research findings. 4 hours/month

5. Trainees (impact on career):

Dates completed	Name	Current Location
1998	Mehrdad Rezaee, MD, PhD	Stanford University, CA
2002	Sohail Khan, MD	Agha Khan University, Pakistan
2000	Lawrence Garcia, MD	BIDMC, Harvard Medical School
2000	Nabil Dib, MD	Arizona Heart Institute
2001	Gilbert Beran, MD	University of Vienna, Austria
2001	Stephane Rinfret, MD	Montreal Heart Institute
2002	Arjuna Mannam, MD	University of Nevada, Las Vegas, NV
2002	Duane Pinto, MD	BIDMC
2002	Simona Kirbis, MD	Slovenia Medical School
2003	Pierre Voisine, MD	BIDMC
2003	Francesco Capelli	Florence Medical School
2003	Yulia Shamis	Hebrew University, Jerusalem
2003	Laurel Donnell-Fink	BIDMC
2003	Audrey Rosinberg	BIDMC
2003	Malik Tamer	BIDMC
2004	Guifu Wu	China, Sun-Yat Sen Univ
2004	Seung Lee	Korea
2005	Joanna Wykrzykowska	BIDMC
2005	Shigetoshi Mieno	Japan

E. Report of Clinical Activities:

1. Interventional cardiology with catheter based cardiovascular revascularization and Critical care cardiology at BIDMC.
2. Patient load in the cardiac catheterization laboratory is in the high volume operator category with 225 complex interventional coronary cases yearly with >50 Peripheral vascular Intervention yearly. Case complexity is high and many cases are referred by

practicing interventional cardiologists for higher skill level intervention and high risk interventions from all over the US.

3. Defining the long-term outcome of stenting, the main device used in interventional procedures.
4. Refining electromechanical mapping, laser myocardial revascularization, and intramyocardial injections techniques including cell based therapy and gene transfer investigation.
5. Perform ethanol ablation as a treatment for hypertrophic cardiomyopathy
6. Perform high risk interventions on no-option patients including unprotected left main intervention, occluded vein grafts, balloon valvuloplasty
7. Treatment of Chronic total occlusion
8. Treatment of PFO using occluder devices
9. Proctoring of interventional cardiologists in intramyocardial injection, rotational atherectomy, distal protection, high risk intervention, Peripheral vascular Disease.
10. Recognition of a Leadership position in the field of clinical angiogenesis, drug delivery, and high risk revascularization, with invited lectures in most interventional cardiology meetings both Nationally and Internationally.
11. Recognition of a Leadership position in the field of Interventional Cardiology, with invited lectures in most interventional cardiology meetings both Nationally and Internationally.
12. Recognition of a Leadership position in the field of clinical Myogenesis and Myocardial regeneration, with invited lectures in most interventional cardiology meetings both Nationally and Internationally.

Part III: Bibliography

Original Articles:

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Undergoing Coronary Bypass Surgery: Results of a Phase I Randomized, Double-Blind, Placebo-Controlled Trial. *Circulation* 1999;100:1865-71.

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